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| EXAMINER | |
|---|---|
| BELYAVSKYI, MICHAIL A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

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Please find below and/or attached an Office communication concerning this application or proceeding.

SM-

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/073,644 | HUDSON ET AL. | |
| | Examiner | Art Unit | |
| | Michail A Belyavskyi | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *20 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *52-100* is/are pending in the application.

4a) Of the above claim(s) *70-84,86,87 and 90-100* is/are withdrawn from consideration.

5)☒ Claim(s) *59,62 and 63* is/are allowed.

6)☒ Claim(s) *52-58,60,61,64-69,85,88 and 89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/16/04; 05/15/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 52-100 are pending.

2. Applicant's election with traverse of Group I, claims 52-69,85,88 and 89 and species of human monoclonal antibody having a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 31-35; 50-66 and 99-108 of SEQ ID NO:6 and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-35, 51-57 and 90-99 of SEQ ID NO:8 in the reply filed on 05/20/04 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the inventions must be both independent and distinct and an undue search burden on the examiner. However, MPEP 803 states that the Inventions be either independent or distinct and a burden on the Examiner if restriction is required.

3. Regarding applicant's comments about undue burden, the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria, indicates that inventions recognized divergent subject matter and that a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Moreover, a prior art search also requires a literature search. All the above establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in the previous Office Action and above.

The requirement is still deemed proper and is therefore made FINAL.

Upon further consideration, the prior art search has been extended to include species of human monoclonal antibody having a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 30-35,50-62 and 99-108 of SEQ ID NO:2 and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-34, 50-56 and 89-97 of SEQ ID NO:4

Claims 70-84, 86-87 and 90-100 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

*Claims 52-69,85, 88 and 89 drawn to an isolated human monoclonal antibody having a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 31-35; 50-66 and 99-108 of SEQ ID NO:6 and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-35, 51-57 and 90-99 of SEQ ID NO:8 and a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 30-35,50-62 and 99-108 of SEQ ID NO:2 and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-34, 50-56 and 89-97 of SEQ ID NO:4 are under consideration in the instant application.*

3. The specification is objected to under 37 CFR 1.821(d) for failing to disclose SEQ ID NOS, for the amino acid sequence disclosed on figures 1-4

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.
*The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

5. Claims 64-69 85, 88 and 89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 64-66 are indefinite in the recitation of " $V_h$3-30.3 gene; $V_k$ L18 or $V_k$ A27 gene" because its characteristics are not known. The use of " $V_h$3-30.3 gene; $V_k$ L18 or $V_k$ A27 gene as the sole means of identifying the claimed gene without providing SEQ ID NOs for said genes renders the claim indefinite because " $V_h$3-30.3 $V_k$ L18 or $V_k$ A27 " is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct product.

B. Claims 67-69, 85 and 88 are indefinite and ambiguous in being dependent upon canceled claim 1.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 52-58, 60-61, 64-69, 85, 88 and 89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated human monoclonal antibody having a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences corresponding to amino acid residues 31-35; 50-66 and 99-108 of SEQ ID NO:6 respectively and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-35, 51-57 and 90-99 of SEQ ID NO:8 respectively or a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 30-35,50-62 and 99-108 of SEQ ID NO:2 respectively and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-34, 50-56 and 89-97 of SEQ ID NO:4 respectively that binds to human CD89 , does not reasonably provide enablement for : (i) any isolated human monoclonal antibody or antigen-binding portion thereof that binds CD89, as recited in claims 52, 56-68; or (ii) an isolated human monoclonal antibody or antigen binding portion thereof comprising a human heavy chain variable region and human light chain variable region wherein the human heavy chain region is at lest 90 % homologous to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable is at least 90 homologous to the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, as recited in claims 60-61 respectively; or (iii) an isolated human monoclonal antibody comprising a heavy chain variable region derived from a human germline $V_H$3-30.3 and a light chain variable region derived from a human germline $V_k$ L18 or $V_k$A27 gene, as recited in claim 64-66. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

The claims as written encompass the genus of antibodies that in addition to simply binding to CD89 have the following functional properties: does not activate complement upon binding to CD89 in vivo; does not block IgA binding to CD89; binding a soluble recombinant CD38.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

There is insufficient guidance and direction as to how to make any isolated human monoclonal antibody or antigen-binding portion thereof that binds CD89, as recited in claims 52, 56-68; or (ii) an isolated human monoclonal antibody or antigen binding portion thereof comprising a human heavy chain variable region and human light chain variable region wherein the human heavy chain region is at lest 90 % homologous to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable is at least 90 homologous to the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, as recited in claims 60-61 respectively; or (iii) an isolated human monoclonal antibody comprising a heavy chain variable region derived from a human germline $V_H$3-30.3 and a light chain variable region derived from a human germline $V_k$ L18 or $V_k$A27 gene that have the required functional properties such as in addition to simply binding to CD89 have the following functional properties: does not activate complement upon binding to CD89 in vivo; does not block IgA binding to CD89; binding a soluble recombinant CD38.

The specification disclosed that positive mAb were screen for and selected based on the following properties: does not activate complement upon binding to CD89 in vivo; does not block IgA binding to CD89; binding a soluble recombinant CD38 ( see page 56 in particular). Only mAb having a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences corresponding to amino acid residues 31-35; 50-66 and 99-108 of SEQ ID NO:6 respectively and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-35, 51-57 and 90-99 of SEQ ID NO:8 respectively or a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 30-35,50-62 and 99-108 of SEQ ID NO:2 respectively and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-34, 50-56 and 89-97 of SEQ ID NO:4 respectively posses said properties.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Because of this lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo *et al* in the Protein Folding problem and Tertiary Structure prediction, 1994, Merz *et al.*, (ed), Birkhauser, Boston, MA, pp.433 and 492-495), it would require an undue amount of experimentation for on of skill in the art to arrive at the claimed any isolated human monoclonal antibody or antigen-binding portion thereof that binds CD89, as recited in claims 52, 56-68; or (ii) an isolated human monoclonal antibody or antigen binding portion thereof comprising a human heavy chain variable region and human light chain variable region wherein the human heavy chain region is at lest 90 % homologous to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable is at least 90 homologous to the amino acid sequence of

SEQ ID NO:4 or SEQ ID NO:8, as recited in claims 60-61 respectively; or (iii) an isolated human monoclonal antibody comprising a heavy chain variable region derived from a human germline $V_H$3-30.3 and a light chain variable region derived from a human germline $V_k$ L18 or $V_k$A27 gene, as recited in claim 64-66.

In view of this unpredictability; the skilled artisan would not reasonably expect an antibody having anything less than 100% identity to human heavy chain region comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable comprising the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8 would in addition to simply binding to CD89 have the following functional properties: does not activate complement upon binding to CD89 in vivo; does not block IgA binding to CD89; binding a soluble recombinant CD38 . Thus the recitation of percent identity language limitations regarding the *sequence length over which the percent identity is required*; does not allow the skilled artisan to make and use: (i) any isolated human monoclonal antibody or antigen-binding portion thereof that binds CD89, as recited in claims 52, 56-68; or (ii) an isolated human monoclonal antibody or antigen binding portion thereof comprising a human heavy chain variable region and human light chain variable region wherein the human heavy chain region is at lest 90 % homologous to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable is at least 90 homologous to the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, as recited in claims 60-61 respectively; or (iii) an isolated human monoclonal antibody comprising a heavy chain variable region derived from a human germline $V_H$3-30.3 and a light chain variable region derived from a human germline $V_k$ L18 or $V_k$A27 gene, as recited in claim 64-66.commensurate in scope with the instant claims without undue experimentation.

In addition, it is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that an isolated human monoclonal antibody or antigen binding portion thereof as defined by the claims which may contain less than the full complement of CDRs from the human heavy chain region comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable comprising the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, have the required binding function. The specification

provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone. Further, the specification does not teach that a functional humanize antibody can be obtained by replacing the CDR regions of an acceptor antibody with the CDRs of a donor antibody. As evidenced by Adair et al. (US Patent 6,632,927) transfer of CDR regions alone are often not sufficient to provide satisfactory binding activity in the CDR-grafted product (col.2 lines 58-61). Panka et al (Proc Natl Acad Sci USA Vol 85 3080-3084 5/88) demonstrate that a single amino acid substiution of serine for alanine results in decreased affinity.

In at least one case it is well known that an amino acid residue in the framework region is involved in antigen binding (Amit et al Science Vol 233 747-753 1986).

Further, a fragment of the heavy chain can be any one of the constant regions (CH1-3) and also may be the hinge region. However, the language also reads on small amino acid sequences which are incomplete regions of the constant region of the antibody. There is no support in the specification for linking the variable region to any or all of the myriad "fragments" which are encompassed within this language. One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed. It is suggested that the specific portion of the human constant region, which the variable region is covalently linked to, be explicitly recited within the claim or this language be removed completely in order to obviate this rejection. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i) any isolated human monoclonal antibody or antigen-binding portion thereof that binds CD89, as recited in claims 52, 56-68; or (ii) an isolated human monoclonal antibody or antigen binding portion thereof comprising a human heavy chain variable region and human light chain variable region wherein the human heavy chain region is at lest 90 % homologous to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable is at least 90 homologous to the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, as recited in claims 60-61 respectively; or (iii) an isolated human monoclonal antibody comprising a heavy chain variable region derived from a human germline $V_H$3-30.3 and a light chain variable region derived from a human germline $V_k$ L18 or $V_k$A27 gene, as recited in claim 64-66 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of

direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 52-58, 60-61, 64-69, 85, 88 and 89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : an isolated human monoclonal antibody having a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences corresponding to amino acid residues 31-35; 50-66 and 99-108 of SEQ ID NO:6 respectively and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-35, 51-57 and 90-99 of SEQ ID NO:8 respectively or a heavy chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 30-35,50-62 and 99-108 of SEQ ID NO:2 respectively and light chain variable region comprising CDR1,CDR2 and CDR3 sequences corresponding to amino acid residues 24-34, 50-56 and 89-97 of SEQ ID NO:4 respectively that binds to human CD89.

Applicant is not in possession of : (i) any isolated human monoclonal antibody or antigen-binding portion thereof that binds CD89, as recited in claims 52, 56-68; or (ii) an isolated human monoclonal antibody or antigen binding portion thereof comprising a human heavy chain variable region and human light chain variable region wherein the human heavy chain region is at lest 90 % homologous to the amino acid sequence of SEQ ID NO:2 or SEQ ID NO: 6 and light chain variable is at least 90 homologous to the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, as recited in claims 60-61 respectively; or (iii) an isolated human monoclonal antibody comprising a heavy chain variable region derived from a human germline $V_H$3-30.3 and a light chain variable region derived from a human germline $V_k$ L18 or $V_k$A27 gene, as recited in claim 64-66 .

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of antibody sequences may be achieved by means of a recitation of a representative number of antibody sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features

constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

*(2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.*

10. Claims 52- 55, 67-69, 85, 88 and 89 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 01/09186 A3 (IDS) or US Patent 6,018031.

WO '186 teaches a human monoclonal antibody 14.1 that is identical to the mAb of the present application and binds to an epitope on CD89 ( see entire document, page 15 in particular). WO'186 teaches a composition comprising antibody 14.1 and pharmaceutically acceptable carrier ( see page 34 in particular). WO' 186 teaches antibody that is a Fab fragment or a single chain antibody and hybridoma producing mAb 14.1 ( see pages 16 and 29 in particular).

US Patent '031 teaches a human monoclonal antibody that is identical to the mAb of the present application and binds to an epitope on CD89 ( see entire document, columns 1 and 7 in particular). US Patent '031 teaches a composition comprising said antibody and pharmaceutically acceptable carrier ( see columns 23 and 24 in particular). Us Patent '031 teaches antibody that is a Fab fragment or a single chain antibody and hybridoma producing mAb 14.1 ( see columns 14 and 28 in particular).

Claims 53-55 are included because the claimed functional limitation would be inherent properties of the antibody taught by WO'186 or by US Patent '031 because the referenced antibody is the same antibody as claimed irrespectively of a method by which it was produced in the absence of evidence of structural difference. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not have the same functional properties as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The references teaching anticipates the claimed invention.

11. The prior art does not teach or suggest the claimed invention recited in claims 59, 62 and 63

12. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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July 13, 2004

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